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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/416,384	10/12/1999	MARTA BLUMENFELD	GENSET.045AU	6101

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1655	21

DATE MAILED: 11/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/416,384	Blumenfeld et al
Examiner	**Art Unit**
Jeffrey Fredman	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 9, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *58, 62, and 73-75* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *58, 62, and 73-75* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on October 9, 2001for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/416,384 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 58, 62, and 73-75 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of polypeptides termed G713 proteins in the specification, antibodies against the G713 proteins, and a method of use of the antibody for detection of the G713 protein.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The only cited utilities identified by the examiner are to detect the protein itself, to make antibodies and to screen drugs. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this specific G713 protein are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence (in the form of published prior art) provided by applicant is argued to support the position that the presence of Glutamine repeats is a substantial utility which is specific to this G713 protein. The prior art, such as Perutz et al (Current Opinion Structural Biol. (1996) 6:848-858), teaches that several diseases are associated with glutamine repeats. This glutamine repeat utility would therefore be based upon the fact that in several other proteins, such as the Huntington's disease gene, or Bulbar muscular dystrophy, glutamine repeats were found to be responsible for the disease state. Applicant thus contends that the presence of these Glutamine repeats in a novel protein would be suggestive of a disease state, perhaps a neurological type disorder.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). If there were evidence of the association of all glutamine repeat containing proteins or the G713 protein itself with any disease state, this evidence might be sufficient to provide a substantial utility. First, there

is NO data in the specification showing expansion of the CAG repeats in this particular protein, and it is the expansion of repeats which is the disease causing element. Many genes comprise glutamine, and many have glutamine repeats. A search of STN revealed that 14,560 sequences in the database which had a 3 repeat sequence of CAGCAGCAG, of which 6,723 sequences were associated with human sequences. Second, not all glutamine repeats are associated with a disease state. For example, Kashima et al (J. Biochem. (1987) 102:725-32) notes "These results suggest that the consecutive glutamine repeats do not play a role in the biological and immunological activities of MIL-2, but that the peptide sequence around them does, and the species hierarchy that MIL-2 does not act on human lymphocyte is not due to the presence of glutamine repeats in MIL-2 (abstract)." Kashima expressly demonstrates that in the MIL-2 protein, glutamine repeats do not play a role, and would not be linked to any biological or functional role of the protein. Thus, glutamine repeats represent one of a number of elements which may or may not cause a protein to be associated with a disease and this element does not support a substantial utility for an unknown protein with unknown function which is not associated with any disease.

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, then the substantial utility of the G713 protein is, at best, a relationship to an association with glutamine repeats. This utility is not specific because Perutz, as noted above, has identified many different proteins with glutamine repeats, all of which are associated with different diseases and Kashima has identified at least one protein not disease associated with glutamine repeats. Thus,

the presence of glutamine repeats does not provide a specific utility because there is no direct or even indirect connection made between any particular utility and the G713 protein. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, there is no disclosure of any condition which can be diagnosed and hence, no specific utility.

Finally, with regard to the utility analysis, the current situation directly tracks Example 4 of the utility guidelines, where a protein of entirely unknown function was characterized as lacking utility.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 58, 62, and 73-75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Nature of Invention

Claims 58, 62 and 73-75 are drawn to a G713 protein and methods of detection of this protein or gene product. The nature of this invention is a macromolecular polymer, in particular,

a protein, with no other associated information. This is an invention in a subject area which is well recognized as unpredictable.

Breadth of the claims

The claims are drawn to the particular protein.

Amount of Guidance in the Specification

The specification discloses the entire sequence of the protein, but identifies no particular use for the protein and the asserted utility is the presence of CAG repeat elements. As noted in the utility rejection above, this utility is not found to be substantial nor specific and consequently, the specification provides NO guidance regarding how to use this protein.

Working Examples

There are NO working examples in which this G713 protein is used in any assay for detection or diagnosis of any disease or any other related utility.

Amount of Guidance in Prior Art

As noted in the utility rejection above, the prior art provides no guidance with regard to the particular function of the G713 protein and does not even provide support or guidance for glutamine repeat containing proteins having a particular use or association. As Kashima et al (J. Biochem. (1987) 102:725-32) notes "These results suggest that the consecutive glutamine repeats do not play a role in the biological and immunological activities of MIL-2, but that the peptide sequence around them does, and the species hierarchy that MIL-2 does not act on human lymphocyte is not due to the presence of glutamine repeats in MIL-2 (abstract)." Kashima

expressly demonstrates that in the MIL-2 protein, glutamine repeats do not play a role, and would not be linked to any biological or functional role of the protein.

Skill in the Art

While no evidence is adduced, the examiner believes the skill in the art would be considered high.

Predictability of the Art

The art in biotechnology, as relates to the association of diseases with particular genes, is highly unpredictable. For example, Applicant argues that a particular chromosomal location is associated with schizophrenia. In Wright et al (Schizophrenia Research (2001) 47:1-12), Wright notes that over 16 studies have been performed which purport to associate HLA chromosomal locations with schizophrenia (Table 2). However, Wright notes that "Two recently reported investigations that controlled for most of the confounders discussed above found no evidence of association of HLA with schizophrenia (page 9, column 1). Thus, if Wright's review article and the two 1999 studies are correct, over 16 different studies published from 1975 to 1996 incorrectly linked schizophrenia and HLA. This strongly supports the unpredictability in this linkage of schizophrenia with chromosomal locations given the conflicting results of over 60 different studies (page 5, column 1).

Quantity of Experimentation

An immense amount of experimentation would be required in order to define whether this protein is associated with any particular disease state. In order to acquire statistically significant

evidence of an association with a neurological or other disease, dozens of patients in each of the many hundreds of different possible disease states would need to be subjected to collection of samples for analysis of their DNA, followed by analysis and the inventive efforts of determining if any association exists. This is a very large quantity of experimentation.

Determination

In view of the unpredictable nature of the invention, the absence of any guidance in the specification for a substantial and specific use, the absence of any working examples in the specification, the negative teachings in the prior art, the extreme unpredictability of the invention, and the large amount of experimentation necessary balanced against the high level of skill in the art and the relatively narrow breadth of the claims, it is concluded that undue experimentation would be required to use this invention as claimed.

Claim Rejections - 35 USC § 102/103

6. The 102/103 rejection is withdrawn in view of the amendment.

Response to Arguments

7. Applicant's arguments filed October 9, 2001 have been fully considered but they are not persuasive.

Applicant argues that the prior art supports a finding of utility. As noted above, this argument is not found persuasive.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman, Ph.D. whose telephone number is (703) 308-6568.

The examiner is normally in the office between the hours of 6:30 a.m. and 4:00 p.m., and telephone calls either in the early morning or the afternoon are most likely to find the examiner in the office.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Jeffrey Fredman
Primary Patent Examiner
Art Unit 1655

November 16, 2001